Comparison of mortality in people with Type 1 and Type 2 diabetes by age of diagnosis

Comparison of mortality in people with Type 1 and Type 2 diabetes by age of diagnosis: An incident population-based study in England and Wales

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Type 2 diabetes has traditionally been considered a disease of middle to later life. Changes in lifestyle, particularly rises in obesity and physical inactivity, combined with increased screening have resulted in a growing number of diagnoses in childhood and early adulthood (1). Studies have found greater life years lost in people with Type 2 diabetes diagnosed in adolescence or early adulthood compared to those diagnosed later in life (2) and a recent systematic review reported mortality declines by 4% for each additional year of age at diagnosis (3). Other studies have suggested that in people with type 2 diabetes in early adulthood, mortality (4), cardiac and micro-vascular disease risk (5) are similar to type 1 diabetes. However, these studies include relatively small cohorts and/or were performed prior to changes in diagnostic criteria and the publication in the late 1990s and early 2000s of trials demonstrating the benefits of lower HbA1c, blood pressure and lipids.

To address the lack of contemporary data on mortality in people with type 2 diabetes compared to those with type 1 an incident cohort from the National Diabetes Audit (NDA) for England and Wales of 35,355 people with type 1 diabetes and 1,408,815 with type 2 diabetes diagnosed between 1st January 2008 and 31st December 2014. They were followed until 31st December 2019 (median follow-up of 8·5 (IQR 6·7-10·4) years for type 1 diabetes and 8·0 (IQR 6·3-9·9) years for type 2 diabetes) (see *Appendix* for full methods).

Amongst those diagnosed between the ages of 20 and 39 years old with type 1 diabetes 74.6% were from White ethnic groups, 5.6% from South Asian ethnic groups and 5.4% diabetes, across differing diagnosed age categories, we analysed from Black ethnic groups compared to 47.5%, 24.8% and 7.5% respectively for those with type 2 diabetes ($p<0.0001$). These differences attenuated as age of diagnosis increased. In people diagnosed aged 20 and 39 years, mean body mass index was 7·6 kg/m^2 higher in those with type 2 diabetes compared to type 1 diabetes (33·8 kg/m^2 compared to 26·2 kg/m^2, $p<0·0001$). As age of diagnosis increased the difference in body mass index between those with type 1 and type 2 diabetes decreased (2·0 kg/m^2 for those 60 years and older at diagnosis). Mean HbA1c was higher in people with type 1 compared to type 2 diabetes at all ages. For those diagnosed aged 20 to 39 years old with type 1 diabetes mean HbA1c was 69·4 mmol/mol (8·5%) compared to 59·9

mmol/mol (7·6%) for those with type 2 diabetes (p<0·0001). For both types of diabetes mean HbA1c was lower in those diagnosed at older ages. Mean systolic blood pressure was higher in people with type 2 compared to type 1 diabetes in all age groups under 60 years old (p<0·0005 for aged 20-39 years, p<0·0001 for 40-49 years and 50-59 years, p=0·26 for 60 years and older). Total cholesterol and eGFR did not vary by type of diabetes among people diagnosed at similar ages (see Table S1).

Direct age-matched comparisons between mortality in people with diagnosed diabetes and those without diabetes were not performed within this analysis. However, mortality rates for women diagnosed aged 20 to 39 years of age were 1·4 and 1.6 per 1000 person years for those with type 1 diabetes and type 2 diabetes, respectively, substantially higher than 0·4 per 1000 person years for women aged 20 to 39 years old in the general population for 2012 . For men diagnosed aged 20-39 years old mortality was 2·6 per 1000 person years for type 1 diabetes and 1·9 per 1000 person years for type 2 diabetes compared to 0·8 per 1000 person years for men aged 20 to 39 years old in the general population in 2012 (See Table S2).

In those with type 2 diabetes, across all ages of diagnosis, mortality from cardiovascular disease was higher amongst men than women. A similar pattern was seen in type 1 diabetes but statistical significance was only found in those diagnosed aged 60 years and older. Women diagnosed with type 2 diabetes under the age of 50 years had higher cancer mortality than men diagnosed with type 2 diabetes at similar ages. (See Table S2 and Figure S1).

Cox proportional hazard models were created to assess the hazard of mortality by type of diabetes after adjustment for established risk factors (see *Appendix* for statistical details). The hazard for all-cause mortality for type 1 compared to men with type 2 diabetes was statistically significantly higher among men for all diagnosis age bands. In contrast, mortality was not statistically significantly different by type of diabetes in women when diabetes was diagnosed under 60 years of age. When diagnosed aged 60 years and older mortality among women with type 1 diabetes was lower than for type 2 diabetes. Similar patterns of risk were seen when diabetic coma and ketoacidosis were

excluded as causes of death. The exception was for women diagnosed with diabetes between 20 and 39 years of age for whom mortality was higher for type 2 diabetes compared to type 1 diabetes (See Figure 1).

There have been few studies directly comparing mortality by type of diabetes and age of diagnosis. An Australian study compared mortality in 354 people with type 2 diabetes to 470 people with type 1 diabetes aged 15 to 30 years between 1986 and 2011 and found a risk factor adjusted HR of 2.0 (95% CI 1.2-3.2) (4). This is higher than the HRs found in our study which may relate to the longer study period and secular trends. Analyses from Sweden suggest that type 2 diabetes diagnosed in adolescence is associated with a loss of life expectancy of over a decade (2), while type 1 diabetes diagnosed between 21 and 30 years old results in approximately 10 years of life lost (6). Unlike our analysis, none of these studies examined for differences in relative mortality by type of diabetes for separately for men and women. One study of people diagnosed with diabetes under the age of 20 years old in the United States identified that females had higher mortality than females in the general population (97.8 compared to 48.1 per 100,000 person years) but males with diabetes had similar crude mortality rates to the general population (84.8 compared to 91.8 per 100,000 person years). However, this study did not analyse sex difference by type of diabetes and therefore more detailed analysis would be required to assess comparability with our analysis (7).

The strength of our analysis lies in the size and contemporary nature of the cohort. Widespread coverage of the NDA during the period of diagnosis (on average data were extracted from 75% of general practices) means that the cohort is likely to be broadly representative of the population of people with diabetes in England and Wales. The inclusion of over 129,000 people diagnosed with diabetes between 20 and 39 years old provides statistical power to investigate differences in medium term mortality in those who develop diabetes in early adulthood. As an incident cohort with all individuals followed up from the date of diagnosis, differing duration of diagnosed diabetes should not influence the results. Longer term study is required to identify how mortality risk compares between type 1 and type 2 diabetes over longer duration which would more accurately reflect lifetime

risk, especially for those diagnosed in early adulthood. By including only people diagnosed with diabetes between 2008 and 2014 this study reflects diagnostic and treatment guidelines during that period.

This analysis has further highlighted that type 1 and type 2 diabetes diagnosed in early adulthood are both high risk conditions. Recently the proportion of people with type 2 diabetes diagnosed in early adulthood has increased, they have poorer risk profiles than those diagnosed at older ages (8, 9) and a very high risk of macro and micro-vascular complications (10). Approaches to reducing the burden of diabetes in young people should focus on primary prevention of type 2 diabetes and on risk factor control following diagnosis of both types of diabetes. Interventional studies are required to identify whether aggressive treatment of risk factors, provision of education and technological advances, such as the newer glucose monitoring devices, might reduce the higher relative mortality in young women with type 2 diabetes, and in men with type 1 diabetes. The high proportions of younger people with type 2 diabetes from ethnic minority groups, particularly those of South Asian heritage, and more socially deprived localities, highlight important target populations for primary and secondary prevention.

Conflicts of interest

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Figure

Figure 1: Forest plot of maximally adjusted HR associated with type 1 diabetes compared to type 2 diabetes by age of diagnosis and sex